DATA EVALUATION RECORD

STUDY 1

CHEM 129059	Imidacloprid (NTN 33893)	§161-2

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 42256376
Anderson, C. 1991. Photodegradation of NTN 33893 in water. Nitokuno Laboratory ID No. 88010. Mobay Report No. 101956. Unpublished study performed by Nitokuno, ESR, Yuki Institute, Ibaraki, Japan; Addendums I and II performed by Bayer AG, Leverkusen-Bayerwerk, Monheim, Germany. The study was submitted by Miles Inc. (formerly Mobay Corporation), Stilwell, KS.

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CONCLUSIONS:

Photodegradation in Water

1. Study MRID #42256376 is acceptable and completely satisfies the photodegradation in water 161-2 data requirement for imidacloprid.

2. Imidacloprid photodegraded rapidly with a first order half-life of approximately 1 hour (calculated environmental half-life of 4.2 hours) in sterile aqueous buffer solutions (pH 7) that were continuously irradiated with an artificial light source (xenon lamp) for up to 2 hours at 23-24.5 C. In contrast, imidacloprid did not

IMIDACLOPRID

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degrade during 2 hours of incubation in the dark. The three photoproducts identified after 120 minutes were NTN 38014, at 16.8-17.5% of applied (also referred to as NTN 33823 and photoproduct 2), a dehydro-imino-degradation product of imidacloprid (photoproduct 4) at 11.8-13.4% of applied, and NTN 33519 (photoproduct 1) at 9.2-10.5% of applied.

METHODOLOGY:

Methylene-labeled [^{14}C]imidacloprid [NTN 33893; 1-((6-chloro-3-pyridinyl)methyl)-4,5-dihydro-N-nitro-1H-imidazol-2-amine; radiochemical purity >99%, specific activity 140-150.68 uCi/mg; Bayer AG, Germany] was added at 5.4 ppm to a filter-sterilized aqueous 0.01 M phosphate buffer solution (pH 7.0). Aliquots (10 mL) of the test solution were transferred to 17 quartz vessels; two of the vessels were collected immediately as time 0 samples. A thermometer was inserted into one of the vessels to record temperatures during irradiation. The 14 remaining vessels were sealed with stoppers; two of the sealed vessels were covered with aluminum foil to serve as dark controls. The sealed vessels, plus the vessel containing the thermometer, were placed in a photolysis apparatus (Heraeus Suntest) and continuously irradiated using a xenon arc lamp (intensity 8.9-9.5 uW/cm^2; wavelengths not specified) equipped with a UV glass filter to eliminate radiation below 290 nm. It was reported that the intensity of the light emitted by the xenon lamp was 1.4 times greater than the intensity of natural sunlight in the range of 270-400 nm. The measured intensity of natural sunlight on a bright day at the Yuki Institute was reported to be 4.1-5.3 uW/cm^2 (wavelengths not specified) during April to June 1988. The samples were maintained at 23-24.5 C by a cooling unit (not further described) attached to the photolysis apparatus. Duplicate vessels containing irradiated test solution were sampled after 15, 30, 50, 70, 95, and 120 minutes of irradiation; the dark control solutions were collected at the final sampling interval.

Following the final sampling interval, aliquots (50 uL) of each sample were analyzed for total radioactivity using LSC. The pH of the 120-minute irradiated solutions was also measured upon sample collection. The remaining portion of each sample was stored under refrigeration (temperature not specified) for an unspecified length of time until further analysis. Aliquots of the solutions were analyzed by one-dimensional TLC on silica gel plates using ethyl acetate:isopropanol (80:8, v:v) to quantitate imidacloprid and its degradate NTN 33519, chloroform:ethanol:acetic acid:water (65:25:12:5, v:v:v:v) to quantitate the degradate NTN 38014, and ethyl acetate:isopropanol:water (65:23:12, v:v:v) or chloroform:-ethanol:acetic acid:water (65:25:12:3.5, v:v:v:v) to confirm identifications. Samples were applied to the TLC plates under conditions of near light exclusion to prevent additional photodegradation, and the plates were developed in darkness. Radioactive areas were visualized using autoradiography and quantified using a linear analyzer; degradates were identified by

comparison to the R_f values of unlabeled reference standards that were visualized under UV (254 nm) light (Appendix 6). Additional aliquots of each sample were analyzed by HPLC using a reverse phase C-18 column in conjunction with UV (210 nm) and radioactivity detection; the mobile phases consisted of gradient elutions using either water:dibutylphosphate (500:1, v:v) at pH 2.82:acetonitrile (80:20, v:v) and water:acetonitrile (50:50, v:v) to quantitate imidacloprid and NTN 33519, or aqueous 0.001 M pentane sulfonate sodium at pH 2.2:1,2,3,4-tetrahydro-9-fluorenone (THF; 95:5, v:v) and THF to quantitate other photoproducts. Radioactive peaks were identified by comparison to the retention times of unlabeled reference standards chromatographed and detected with UV absorbance. Photoproduct identifications were confirmed using electron impact and chemical ionization MS.

An additional experiment was conducted to isolate and identify photoproduct 4. A 1000-mL sterile aqueous 0.01 M phosphate buffer solution (pH 7.0) containing methylene-labeled [^{14}C]imidacloprid plus unlabeled imidacloprid, at approximately 10 ppm, was continuously irradiated in the Suntest photolysis apparatus; the intensity of the xenon lamp was measured at 11.8-12.4 mW/cm^2 between 300-400 nm using a UV-light meter. The incubation temperature was not reported. The test solution was collected after 3.5 hours of irradiation and lyophilized; the resulting residue was redissolved in water. An aliquot of the concentrated sample was purified and fractionated by HPLC on a reverse phase column in conjunction with UV (210 nm) and radioactivity detection; the mobile phase consisted of a gradient elution combining aqueous 0.005 M pentane sulfonic acid (pH 2.2):THF (95:5, v:v) and THF. The fraction containing photoproduct 4 was collected, concentrated, and purified twice by TLC on silica gel cards using chloroform:methanol:water:formic acid (65:25:1:1, v:v:v:v); following each development, the sample was extracted from the silica gel with methanol. The isolated photoproduct was compared to the initial irradiated solution using HPLC, then analyzed by NMR and electron impact and chemical ionization MS.

DATA SUMMARY:

Methylene-labeled [^{14}C]imidacloprid [NTN 33893; 1-((6-chloro-3-pyridinyl)-methyl)-4,5-dihydro-N-nitro-1H-imidazol-2-amine; radiochemical purity >99%], at 5.4 ppm, photodegraded rapidly with a calculated half-life of 57 minutes in sterile aqueous 0.01 M phosphate buffer solution (pH 7.0) that was continuously irradiated with a UV glass-filtered xenon arc lamp (intensity 8.9-9.5 uW/cm^2; wavelengths not specified) at 23-24.5 C for 120 minutes; the study author calculated a theoretical half-life of 4.2 hours in natural sunlight. It was reported that the intensity of the lamp was 1.4 times greater than natural sunlight in the range of 270-400 nm. In the dark control solution, [^{14}C]imidacloprid comprised 99.2-99.7% of the recovered radioactivity (HPLC analysis) at the 120-minute postirradiation sampling (Appendix 12). The major photoproduct in the irradiated solution was

NTN 38014 (photoproduct 2, also referred to as NTN 33823).

As determined by HPLC of the test solution after 120 minutes of irradiation, imidacloprid comprised 26.2-31.2% of the recovered radioactivity, NTN 38014 comprised 16.8-17.5%,

a dehydro-imino-degradation product of imidacloprid (photoproduct 4)

comprised 11.8-13.4%,

NTN 33519 (photoproduct 1)

comprised 9.2-10.5%, and two unidentified HPLC peaks, photoproducts 3 and 5, comprised 9.6-10.6% and 7.9-8.9%, respectively (Appendices 12, 21 and 22). At 120 minutes postirradiation, the pH of the irradiated test solutions was 7.05-7.08. Material balances ranged from 98.0 to 101.8% of the applied (Appendix 16).

COMMENTS:

1. The unidentified HPLC peak-designated photoproduct 3 comprised a maximum of 12.8-14.5% of the recovered radioactivity at 95 minutes postirradiation. The study author reported that further chromatographic investigations of the fraction containing photoproduct 3 determined that it was composed of several components.

   In addition, 12.8-13.6% of the radioactivity recovered following HPLC was not accounted for in the 120-minute irradiated samples (Appendix 22).

2. In general, the EFGWB requires that more than one radiolabel be used on a two ring system molecule. However, because of the extensive spectroscopic analysis (NMR, and MS) on isolated/purified degradates and excellent mass balences, there will be no need for further studies on a pyridinyl ring-labeled or imidazole ring-labeled [^{14}C]imidacloprid.

3. Sampling intervals for irradiated and dark control solutions were reported in terms of minutes postirradiation rather than in terms of minutes posttreatment. The actual length of time elapsed between preparation of the test solution and commencement of sample irradiation could not be determined. Since imidacloprid does not degrade in pH 7 buffer solution when maintained in darkness, reporting the sampling intervals in terms of time postirradiation does not have any adverse effect on this review of the study; however, reporting the sampling intervals in terms of time posttreatment is standard practice.

4. The study author reported that the intensity of the xenon light source was measured using a UV-radiometer prior to and after irradiation of the samples; however, the distance from the light

source to the radiometer and the distance from the light source to the vessels containing the test solution were not reported. The intensity of the xenon lamp used at Yuki Institute was reported to be 8.9-9.5 uW/cm^2, but the wavelengths at which the light intensity was measured were not reported; the intensity of the xenon lamp used at Bayer AG in Germany was reported to be 11.8-12.4 mW/cm^2 at 300-400 nm, which is approximately 1000-fold greater in intensity. The manufacturer's specifications for the artificial light source used at Yuki Institute were provided and compared to midday summer sunlight at 40° N latitude in the range of 270-400 nm; using this information, the study author reported in the text that the intensity of the light emitted by the xenon lamp was 1.4 times greater than the intensity of natural sunlight.

5. The comparison of the artificial light source to natural sunlight was incomplete. In the study text, the measured intensity of natural sunlight on a bright day at Yuki Institute (approximately 35° N latitude) was reported to be 4.1-5.3 uW/cm^2 (wavelengths not specified) during April to June 1988. It was not reported if the xenon lamp and natural light intensities were measured with the same radiometer. Important information regarding the light intensity was not reported, including the wavelengths at which the natural light was measured, the actual measured intensities, and the time of day the intensity was measured. It was reported that the intensity of the light emitted by the xenon lamp was 1.4 times greater than the intensity of natural sunlight in the range of 270-400 nm; Appendix 23 presents information on the light intensity of the lamp and midday midsummer sunlight at 40° latitude from 270-400 nm.

6. The figure (Appendix 4) purportedly showing the irradiation apparatus was totally inadequate. Thus, it was not clear how the temperature of the photolysis apparatus was maintained; the study author reported only that the Suntest photolysis apparatus was connected to a cooling unit which was not described.

7. The study author reported that test solutions were stored refrigerated (temperature unspecified) prior to analysis. The length of time that each sample was stored was not specified, so it could not be determined whether storage had any effect on the results.

8. An absorption spectrum of 1.05 ppm imidacloprid in water is presented in Appendix 8; the study author reported that the test substance has an absorption maximum at 269 nm. The absorption spectra of 1.05 ppm imidacloprid at pH 5 and 9 (buffer solutions not described) did not differ significantly from the spectra of imidacloprid in water (Appendix 9). An absorption spectra of imidacloprid in pH 7 buffer solution was not provided.

9. The solubility of imidacloprid in water at 20 C was reported to be 580 ppm (0.58 g/L).

10. Photoproduct 2 is identified as NTN 38014 (Appendix 18 of main study) and NTN 33823 (Appendix 14 of Addendum II). In Appendix 6 of Study 3 (MRID 42256378), NTN 38014 is reported to be the free base of NTN 33823. In addition, the degradate NTN 33519 (photoproduct 1) in this study is referred to as DIJ 9817 in the anaerobic aquatic study (Appendix 6 in Study 3, MRID 42256378). Changing the reference number of the same structure from study to study is illogical and confusing; the registrant should provide chemical names for all degradates of imidacloprid.

11. In an attempt to identify photoproducts, the registrant conducted experiments in which test solutions containing 102.7 ppm of methylene-labeled [^{14}C]imidacloprid plus unlabeled imidacloprid were continuously irradiated in the Suntest photolysis apparatus for 21 hours (Addenda I and II). However, since the concentration of the test solution, the length of irradiation, and the light intensities differed from those of the initial 2-hour photolysis study, there is no way to determine if what was observed in the 21-hour studies is comparable to what occurred in the 2-hour study. Although it is acceptable to conduct studies for the sole purpose of generating additional material for degradate characterizations, the conditions between those studies and the initial definitive study must be roughly equivalent in order to make valid comparisons.

    Based on the results of one of the high concentration 21-hour studies, it was proposed that three minor photodegradates (WAK 5031, WAK 4126, and GSE 2712) may have coeluted with photoproducts 2 and 4 in the initial study; it was estimated that the degradates comprised $\leq$1.6% of the applied radioactivity in the initial study (Addendum II).

12. In a separate experiment, aliquots of a 10 ppm aqueous solution of unlabeled imidacloprid (purity >99%) were placed in quartz vessels, sealed, and irradiated in natural sunlight in a greenhouse located at Yuki Institute (approximately 35° N latitude); there was no dark control. The irradiated solutions were sampled at 0, 4, and 7 hours posttreatment and analyzed for imidacloprid by reverse phase HPLC using UV detection. The study author reported that 60% of the parent imidacloprid had degraded after 4 hours of irradiation, but no data were provided.

13. Methods are presented in Appendix 5 indicating that microbiological analyses were performed using the test solutions to assess sterility; however, no results were provided. Since the experiments were of such short duration, sterility would not be a factor.

14. The registrant reported that imidacloprid [NTN 33893; 1-((6-chloro-3-pyridinyl)methyl)-4,5-dihydro-N-nitro-1H-imidazole-2-amine] is a broad spectrum, systemic insecticide. The proposed maximum use rates for food and non-food crop uses are 0.5 lb ai/A or 500-560 g/ha (Study 4, MRID 42256379).

15. It is stated in the list of chemicals that PIC D is dibutylphosphate.

Pages 9-26 Access to FIFRA registration data is restricted under FIFRA section 10(g)